



SCIENTIFIC EDITORIAL

NT-BNP/BNP for screening left ventricular hypertrophy in hypertension: What else?☆

L'utilisation de NT-BNP/BNP pour le dépistage de l'hypertrophie ventriculaire gauche dans le cas d'hypertension : quoi d'autre ?

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The therapeutic strategies for treating hypertension depends on the patient global cardiovascular risk; this risk is not only associated to the severity of increased blood pressure but also to the presence of other cardiovascular risk factors and of target organs damage such as left ventricular hypertrophy (LVH). Screening for left ventricular hypertrophy is therefore a desirable goal in the management of hypertensive patients, but ECG has a limited value and echocardiography is not recommended on a routine basis for limited access and cost-effectiveness reasons [1,2]. Thus, there is a need for surrogate markers.

B-type natriuretic peptides (BNP or NT-proBNP) have been extensively studied in recent years as a clinical marker of heart overload. BNP is produced mainly by the ventricular myocardium in response to increased intracavitary pressure and wall stress. Plasma BNP/NT-proBNP measurement has become an accepted method for diagnosing heart failure [3]. Moreover, the application of this biochemical marker for guiding the treatment in chronic heart failure has shown promising results and BNP plasma level also provides prognostic information in CHF or at discharge after treatment of acute decompensation.

However, the use of plasma BNP for the diagnosis of left ventricular dysfunction or hypertrophy in the general population or in hypertensive patients has provided more controversial results [4,5]. In this issue of the journal [6], Mouly-Bertin et al. found a good accuracy for plasma NT-proBNP to screen for LVH in 93 hypertensive patients, especially in women with an 88% sensitivity and specificity and positive and negative predictive values of 76 and 95%, respectively. Beside LV mass index, they also found that 24-h systolic

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ambulatory blood pressure and gender were independent determinants of NT-proBNP. Surprisingly, they reported no statistical interaction with age, creatine clearance, treatments or diastolic dysfunction. It is noteworthy that the patients of the study represent a selected population with a very high prevalence of LVH (44%). Moreover, the fact that about 25% of the patients (30/123) have been excluded from the initial analysis subsequently to the echocardiographic findings represents an important limitation for the application of the results in a hypertensive population. These latter facts together with the limited number of patients compared to previous negative studies should have incited the authors to be more cautious regarding their conclusions.

Mechanisms of increased plasma BNP in hypertension

Most studies have shown that LVH was associated with a significant increase in plasma BNP [7]. However, compared to patients with definite heart failure, the amplitude of this elevation is much lower and in the range of elderly "normal" patients especially. The precise mechanisms of BNP/NT proBNP elevation in hypertension are not fully understood: it can reflect both cardiac structural or functional changes such as LVH or LV systolic or diastolic dysfunction [8] but also their hemodynamic consequences such as elevated intracardiac pressures. In hypertension, elevated plasma BNP can be the consequences of increase systolic wall stress or increase LV filling pressure and diastolic wall stress [9] and its impact on left atrial stretch together with the increase in LV mass. We can speculate that for a given filling pressure the higher the mass, the higher amount of B type natriuretic peptides can be released. However, in another sense if we assume that the main mechanism of secretion is myocyte stretch, a higher wall thickness could also contribute to normalize diastolic or systolic wall stress (Laplace law). Therefore, we can speculate that BNP/NT-proBNP release is probably the result of the balance between these different mechanisms.

Factors influencing BNP secretion

All the studies performed in the general population have shown that plasma BNP/NTproBNP increase with age and are higher in female than in male in "normal" subjects. Therefore, when defining threshold for LVH, age and sex must surely be taken into account [10].

Moreover, many other cardiac or non cardiac factors may influence B type natriuretic peptide secretion: among cardiac factors, heart failure, LV systolic or diastolic dysfunction or more simply increase in LV filling pressure with normal systolic function, and also valvular heart disease, atrial fibrillation. Several studies have emphasized the interaction between diastolic dysfunction as a marker of increased filling pressure and LVH to explain the increase of plasma BNP/NT-proBNP in hypertension [8]. On the opposite, LVH alone with relatively low cardiac filling pressures achieved spontaneously or with the use of diuretics or vasodilators can be associated with normal BNP/NT-proBNP levels, as it is observed in some heart failure patients with LV

systolic dysfunction [11]. On the opposite, beta-blockers by increasing the diastole duration on a steeper filling pressure volume curves could increase the levels of plasma natriuretic peptides by reaching higher end diastolic pressure [12,13]. Primary or secondary pulmonary hypertension (even in the absence of left side pathology) can also participate in an increase of plasma BNP/NT-proBNP. Finally, among non cardiac factors, renal dysfunction is an important determinant of plasma BNP/NT-proBNP elevation [14], due to both reduced renal natriuretic peptides clearance and expanded plasma volume, and this factor should certainly be taken into consideration in hypertensive patients. In conclusion, it is wise to think that an increase in plasma BNP/NT-proBNP is a non specific marker of "cardiorenal distress", which usually requires additional investigation [4].

Could BNP/NT-proBNP replace echocardiography in hypertension?

The authors conclude that ECG and NT-proBNP should totally replace echocardiography in women and that echocardiography should be restricted to men with a negative ECG and a negative NT-proBNP test. These assumptions need to be discussed carefully: in fact, we think it is useful to perform an echocardiography when plasma BNP/NT-proBNP is increased because it is important to find out what is wrong with the heart. Beside LVH, echocardiography could detect abnormal systolic function and segmental abnormal wall motion related to ischemic cardiac disease. It could also assess the type of LVH, eccentric or concentric, which seems related to different pronostic values. On the opposite, a normal ECG and a normal plasma BNP/NTproBNP, in the absence of functional or clinical cardiac signs, are usually associated with a good prognosis, and this probably could avoid the use of echocardiography even if it can not totally rule out LVH.

In conclusion, although the contribution of Mouly-Bertin et al. is interesting, we actually think that plasma BNP/NT-proBNP are non-specific markers of cardiac or renal dysfunction. In the setting of hypertension, it is illusory to think it should replace echocardiography. Moreover, the economic implications of measuring BNP/NT-proBNP in all hypertensives patients and its impact on healthcare should deserve careful evaluations before being recommended routinely.

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